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Published in:
B M J Open

DOI:
[10.1136/bmjopen-2017-017436](https://doi.org/10.1136/bmjopen-2017-017436)

Publication date:
2017

Document version
Publisher's PDF, also known as Version of record

Document license:
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Citation for published version (APA):
Skou, S. T., Lind, M., Hölmich, P., Jensen, H. P., Jensen, C., Afzal, M., Jørgensen, U., & Thorlund, J. B. (2017). Study protocol for a randomised controlled trial of meniscal surgery compared with exercise and patient education for treatment of meniscal tears in young adults. *B M J Open*, 7(8), [e017436]. <https://doi.org/10.1136/bmjopen-2017-017436>

BMJ Open Study protocol for a randomised controlled trial of meniscal surgery compared with exercise and patient education for treatment of meniscal tears in young adults

Søren Thorgaard Skou,^{1,2} Martin Lind,³ Per Hölmich,⁴ Hans Peter Jensen,⁵ Carsten Jensen,^{6,7} Muhammad Afzal,⁸ Uffe Jørgensen,⁹ Jonas Bloch Thorlund¹

To cite: Skou ST, Lind M, Hölmich P, *et al.* Study protocol for a randomised controlled trial of meniscal surgery compared with exercise and patient education for treatment of meniscal tears in young adults. *BMJ Open* 2017;7:e017436. doi:10.1136/bmjopen-2017-017436

► Prepublication history and additional material are available online. To view, these files please visit the journal (<http://dx.doi.org/10.1136/bmjopen-2017-017436>).

Received 22 April 2017

Revised 24 June 2017

Accepted 11 July 2017

ABSTRACT

Introduction Arthroscopic surgery is a very common orthopaedic procedure. While several trials have investigated the effect of knee arthroscopy for middle-aged and older patients with meniscal tears, there is a paucity of trials comparing meniscal surgery with non-surgical treatment for younger adults. The aim of this randomised controlled trial (RCT) is to investigate if early arthroscopic surgery is superior to exercise therapy and education, with the option of later surgery if needed, in improving pain, function and quality of life in younger adults with meniscal tears.

Methods and analysis This is a protocol for a multicentre, parallel-group RCT conducted at six hospitals across all five healthcare regions in Denmark. 140 patients aged 18–40 years with a clinical history and symptoms consistent with a meniscal tear, verified on MRI, found eligible for meniscal surgery by an orthopaedic surgeon will be randomly allocated to one of two groups (1:1 ratio). Participants randomised to surgery will undergo either arthroscopic partial meniscectomy or meniscal repair followed by standard postsurgical care, while participants allocated to exercise and education will undergo a 12-week individualised, supervised neuromuscular and strengthening exercise programme and patient education. The primary outcome will be difference in change from baseline to 12 months in the mean score on four Knee Injury and Osteoarthritis Outcome Score subscales, covering pain, symptoms, function in sports and recreation and quality of life (Knee Injury and Osteoarthritis Outcome Score (KOOS₄)) supported by the individual subscale scores allowing clinical interpretation. Alongside, the RCT an observational cohort will follow patients aged 18–40 years with clinical suspicion of a meniscal tear, but not fully eligible or declining to participate in the trial.

Ethics and dissemination Results will be presented in peer-reviewed journals and at international conferences. This study is approved by the Regional Committees on Health Research Ethics for Southern Denmark.

Registration details ClinicalTrials.gov (NCT02995551).

BACKGROUND

Knee arthroscopy is a very commonly performed orthopaedic procedure.^{1 2} According to

Strengths and limitations of this study

- This study addresses an important evidence gap regarding the optimal treatment strategy of meniscal tears in young adults.
- The multicentre design including patients from all healthcare regions of Denmark comparing two feasible and clinically relevant treatment strategies will support external validity and implementation.
- Owing to the type of interventions, blinding of the patients and treatment providers is not possible.

the previous reports, around 1 million procedures are performed annually in the USA³ and 150 000 procedures in the UK,⁴ with most procedures involving meniscal tears.^{3 4}

Systematic reviews and meta-analyses of randomised trials show no better effect of arthroscopic partial meniscectomy (APM) for middle-aged and older patients with degenerative meniscal tears compared with placebo surgery or in addition to exercise.^{5 6} In addition, meniscal surgery is associated with risk of adverse events.⁵ A recent randomised controlled trial (RCT) confirmed that exercise therapy is a valid treatment option for middle-aged patients with degenerative meniscal tears as no difference was observed in patient-reported outcomes, when comparing APM surgery with exercise therapy head-to-head.⁷ However, no RCTs have compared arthroscopic meniscal surgery for patients aged 40 years or younger with non-surgical treatments.⁸

In contrast to middle-aged and older people with degenerative meniscal tears most tears in younger adults are of traumatic origin from a work-related or sports-related trauma.⁹ Symptoms associated with meniscal tears are considered to be resolved with



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For numbered affiliations see end of article.

Correspondence to

Dr Søren Thorgaard Skou;
stskou@health.sdu.dk

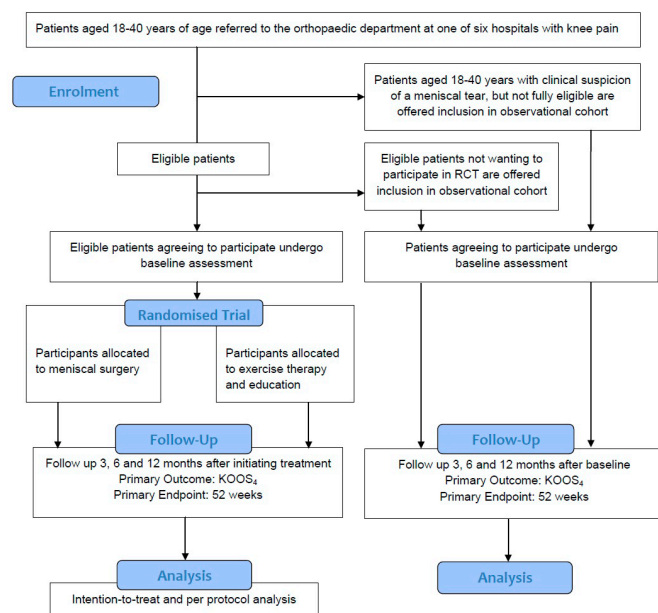


Figure 1 Patient flow through the study. RCT, randomised controlled trial; KOOS₄, the mean score for the Knee Injury and Osteoarthritis Outcome Score subscales pain, symptoms, function in sports and recreational activities (Sport/Rec) and quality of life (QOL).

surgery (ie, repair or resection), but exercise might be a valid treatment option considering previous trials in middle-aged and older patients.^{5 7} Evidence from more severe traumatic knee injuries such as anterior cruciate ligament (ACL) tears suggest that more than half of ACL-injured patients can obtain satisfactory knee function with structured and supervised exercise therapy as first-line treatment before considering surgery.¹⁰

The aim of this RCT is to investigate if early arthroscopic meniscal surgery is superior to individualised supervised exercise therapy and patient education, with the option of later surgery if needed, in improving pain, function and quality of life in young patients (18–40 years of age) with meniscal tears. We hypothesise that patients randomised to surgery will improve significantly more in pain, function and quality of life after 12 months than those randomised to exercise and patient education.

METHODS AND ANALYSIS

Study design

This study protocol (version 2, 30 March 2017) describe the design of a multicentre, parallel-group RCT (1:1 ratio) conducted at six orthopaedic departments across all five healthcare regions in Denmark.

The study protocol conforms with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)¹¹ while the RCT will conform to the Consolidated Standards of Reporting Trials (CONSORT) statement for reporting RCTs.¹²

The orthopaedic departments at Aalborg University Hospital, Aarhus University Hospital, Lillebælt Hospital

(Kolding), Næstved Hospital and Copenhagen University Hospital (Amager-Hvidovre) will recruit patients for the study.

The study is registered at ClinicalTrials.gov in December 2016 (NCT02995551) and enrolment started at the first hospital in January 2017 and at the last hospital in April 2017 and recruitment is expected to finalise in June 2018.

Patients

One hundred and forty patients fulfilling the eligibility criteria below will be included.

Inclusion criteria

- ▶ Adults aged 18–40 years with knee pain.
- ▶ Clinical history and symptoms consistent with meniscal tear and meniscal tear verified on MRI.
- ▶ Deemed eligible for meniscal surgery (ie, repair or resection) by the examining orthopaedic surgeon.
- ▶ Willing to participate in 12 weeks of supervised exercise twice a week and undergo surgery for the meniscal tear as soon as possible.

Exclusion criteria

- ▶ Previous knee surgery on the affected knee.
- ▶ Clinical suspicion (acute locking of knee and/or extension deficit) of displaced bucket-handle tear confirmed by MRI.
- ▶ Fracture of the affected extremity within the previous 6 months.
- ▶ Complete rupture of one or more knee ligaments.
- ▶ Participation in supervised systematic exercise for knee problems within the last 3 months prior to recruitment.
- ▶ Other reasons for exclusion (unable to understand Danish, mentally unable to participate, etc).

Recruitment procedure

The overall trial flow is outlined in [figure 1](#). Patients referred to the orthopaedic department at one of the six hospitals and complying with the eligibility criteria will be invited to participate in the RCT study. Orthopaedic surgeons, nurses and physiotherapists involved in recruitment have been trained and instructed in the recruitment procedure in order to maximise the recruitment rate.

Oral and written information about the study will be provided by the examining orthopaedic surgeon and/or by a nurse or physiotherapist at the six different recruiting orthopaedic departments in an undisturbed room during consultation at the hospital. The study information is also available in a video for the patient to watch at home or at the hospital, before deciding to participate or not. Patients are recommended to take at least 24 hours to consider and discuss participation with a relative or a lay representative before deciding on participation in the study.

Either the local project worker or a central study coordinator (depending on local differences at the hospitals) will contact the patient and ask whether they are willing



to participate in the study. If so, written informed consent will be obtained (see online supplementary file 1).

Randomisation procedure and concealment of allocation

Patients fulfilling eligibility criteria and willing to participate will be randomised after baseline assessment (1:1 allocation ratio). A priori, an independent statistician has prepared a computer-generated randomisation schedule in random-sized permuted blocks of four or six patients stratified by hospital and gender to ensure that the number of participants receiving the two interventions is closely balanced within each stratum. The allocation numbers will be concealed in opaque sealed envelopes prepared by a central study coordinator. The envelopes will only be accessible by the central study coordinator, only opening them after informed consent and baseline measures have been obtained.

Blinding

An independent statistician blinded to group allocation will perform the primary RCT analysis. To reduce risk of interpretation bias, blinded results from the analyses (Group A compared with Group B) will be presented to all authors, who will agree on two alternative written interpretations before the data manager unblinds the randomisation code.¹³

Observational cohort

Patients fulfilling all eligibility criteria, but unwilling to participate in the randomised study, and patients aged 18–40 years with a clinical history and symptoms consistent with a meniscal tear, but not fulfilling the other eligibility criteria, are invited into an observational cohort with the same self-reported questionnaires as applied in the RCT, but following usual clinical practice. Written informed consent will be obtained for all cohort participants.

Interventions

Patients will be randomised to one of two treatments initiated as soon as possible after randomisation.

Arthroscopic meniscal surgery

Arthroscopic meniscal repair or resection will be conducted at the discretion of the operating surgeon at one of the six hospitals. The specific surgical procedure (ie, repair or resection) cannot be determined before the surgeon has visual confirmation about the exact knee pathology and extent of the meniscal tear at arthroscopy. Patients will receive the standard postoperative rehabilitation depending on type of surgery (ie, repair or resection). A standard leaflet with exercises will be given to patients undergoing APM at all surgery sites. Patients undergoing meniscal repair will follow a hospital-specific rehabilitation regimen to improve the external validity of the study findings. The hospital-specific regimes range from postsurgical control of range of motion and instruction in a standardised postsurgical exercise programme to referral to supervised, knee-related exercises focusing

on increasing range of motion and strength, most often in patients with reduced range of motion or not able to activate vastus medialis following meniscal repair.

Exercise therapy and patient education

Patients allocated to exercise therapy and patient education will twice weekly participate in a 12-week individualised, supervised exercise programme (approximately 60–90 min/session) tailored to 18–40 years old patients with meniscal tear. The content of the exercise therapy programme was guided by available evidence from patients with other types of knee injuries and osteoarthritis^{7 10 14–17} and developed in close collaboration with experienced physical therapists and pilot patients.¹⁸ Each exercise session includes a warm up period of 5 min on a stationary bike and neuromuscular and strengthening exercises focusing on the lower extremities. If needed during the first weeks, two exercises focusing on reducing swelling and increasing range of motion is included. The neuromuscular exercises are individualised based on 2–6 levels of difficulty and performed with 10–15 repetitions in 2–3 sets. The strengthening exercises are initially performed in two sets of 15 repetitions, progressing to three sets of 12, three sets of 10 and three sets of eight repetitions.¹⁸ The exercise therapy programme was tested in a pilot study¹⁸ and reported according to the Consensus on Exercise Reporting Template (CERT).¹⁹ The pilot study included six patients fulfilling the same eligibility criteria as for the present RCT. The exercise programme was found feasible with few short-lasting periods of increased pain or other symptoms during the exercises and marked self-reported improvements after 12 weeks.¹⁸ For full details about the exercise programme please refer to Skou and Thorlund.¹⁸

The patient education was developed to support the exercise therapy programme and build motivation and capability to sustain the exercise after the 12-week programme. It was adapted, through interviews with pilot study participants, based on our experiences from the Good Life with osteoArthritis in Denmark (GLA:D) programme for patients with knee and hip pain.¹⁷ See further description in [table 1](#) according to the Template for Intervention Description and Replication (TIDieR).²⁰

The exercise therapy programme and patient education will be delivered at one of 16 private physiotherapy clinics and municipalities geographically related to the six hospitals. All physiotherapists are part of the GLA:D infrastructure and used to deliver and supervise exercise therapy in a similar manner as in the present study. Furthermore, all physiotherapists attended a specific half-day course to be certified to deliver the specific treatment in this trial.

Crossover and discontinuation

Crossovers are common in studies randomising patients to surgical or non-surgical treatment.^{10 14 21} Based on previous experience, a number of precautions have been taken to reduce crossover and discontinuation. Within

Table 1 Overview of the patient education*

Item	Description
1. Brief name	DREAM patient education
2. Why	The education programme was adapted through interviews with pilot study participants from our experiences from the GLA:D programme for patients with knee and hip pain. ¹⁷ The programme will support the exercise therapy programme and build motivation and capability to sustain the exercise after the 12-week programme.
3. What materials	A Power Point presentation supported by a manual for physiotherapists describing what to say and how to respond to specific queries.
4. What procedures	In the initial phase of the 12-week programme, the patients will be given information on meniscal tears, symptoms, treatments and prognosis and focus on individual goals. At the end of the 12 weeks, a session focusing on sustaining the motivation for continuous exercise, return to sports and other activities and future goals will be given.
5. Who provided	The education will be delivered by the physiotherapists supervising the exercise programme. The physiotherapists have all undergone training in the GLA:D programme and study-specific training.
6. How	Delivered face to face in groups and individually.
7. Where	At private physiotherapy clinics and municipalities across Denmark.
8. When and how much	In the beginning and at the end of the 12-week programme in two or more sessions. Total duration is expected to be 30–45 min. During the exercise, programme patients and physiotherapists will discuss subjects related to the education and individual patient goals.
9. Tailoring	The patients will set individual goals that will be followed up after the 12-week programme.
10. Modifications	Modifications will be reported (if any).
11. How well (planned)	The physiotherapists have received training before the study was initiated in how to deliver and supervise the education and exercise therapy programme.
12. How well (actual)	This will be reported in the primary paper.

*Described according to the Template for Intervention Description and Replication (TIDieR).²⁰

DREAM, Danish Rct on Exercise versus Arthroscopic Meniscal surgery for young adults; GLA:D, Good Life with osteoArthritis in Denmark.

1 week from randomisation, the central study coordinator will call patients and talk to them about their participation in the study and what is going to happen during the study. The physiotherapists have been trained to encourage patients to stay in the exercise and education group at least until after the 12-week programme has been completed. This is important as it often require around 6 weeks before important improvements in pain are reported.²² Results from the pilot study suggest that clinically important improvements might not occur until after 8–10 weeks.¹⁸ A similar time frame of improvements can be expected for patients undergoing surgery. Patients insisting to crossover to surgery or discontinue their participation will be contacted by the central study coordinator regarding their reasons for crossover or discontinuation. If needed, they will be reassessed by an orthopaedic surgeon. The reason for each crossover and discontinuations will be registered. Patients crossing over will remain in the study and will be included in the intention-to-treat analyses.

The general crossover criteria from exercise and education to surgery are:

- score of 25 or less on the pain and/or quality of life (QOL) subscale on the Knee Injury and Osteoarthritis Outcome Score (KOOS)^{23 24} or,

- agreement between patient and orthopaedic surgeon that surgery is necessary.

Data collection procedure

Data will be collected at baseline, at surgery (for those randomised to surgery) and 3, 6 and 12 months after initiating the treatment. All but the physical performance tests will be collected using online-based questionnaires or Short Message Services (SMS). Physical performance measures will be assessed at the hospitals by project workers specifically trained in the test protocol. Please refer to [table 2](#) for an overview of collection of the different outcomes.

Outcomes

Baseline characteristics

Patient characteristics such as height, weight, pain location, symptom duration and symptom onset will be collected. Symptom duration and symptom onset will be answered by the questions: 'How long have you had your knee pain/problems for which you are now having treatment?' with six response options ranging from 'less than 2 weeks' to 'more than 24 months', 'How did the knee pain/problems for which you are now having treatment develop?' with three response options 'The pain/

**Table 2** Overview of data collection*

	Baseline	Surgery	3 month	6 month	12 month
Baseline characteristics					
Age	X				
Gender	X				
Study knee	X				
Height	X				
Weight	X		X	X	X
Education level	X				
Employment status	X				
Prior treatment of knee	X				
Smoking status	X				
Comorbidities	X				
Symptom duration	X				
Symptom onset	X				
Joint line tenderness (medial and lateral)	X				
Thessaly's test (at 20° knee flexion)	X				
McMurray's test	X				
Surgery information					
ISAKOS meniscal tear classification		X			
Surgery reports		X			
Patient reported outcomes					
KOOS	X		X	X	X
WOMET	X		X	X	X
EQ-5D	X		X	X	X
Physical activity level	X		X	X	X
Sports participation	X		X	X	X
Pain location	X		X	X	X
Symptoms of catching and locking	X		X	X	X
Knee instability	X		X	X	X
Global perceived effect			X	X	X
Patient acceptable symptom state			X	X	X
Treatment failure					X
Physical performance tests					
Isometric muscle strength	X		X		X
Knee-bend test	X		X		X
Jump performance (two tests)					X
Adverse events					
Patient-reported at follow-up			X	X	X
Medical record review					X
Treatment-related variables					

Continued

Table 2 Continued

	Baseline	Surgery	3 month	6 month	12 month
Compliance with and progression of exercise (only for patients in the exercise group, registered after each session)			X		
Participation in postsurgery exercise (only for patients in the surgery group)			X		
Surgery and/or other treatments during follow-up					X

*Some of the other outcome measures will be collected using Short Message Services and are not shown as they follow a different follow-up pattern.

Data in the surgery column are only collected for patients undergoing surgery.

EQ-5D, EuroQol Group 5-Dimension Self-Report Questionnaire; ISAKOS, International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine, classification of meniscal tears questionnaire; KOOS, Knee injury and Osteoarthritis Outcome Score; WOMET, Western Ontario Meniscal Evaluation Tool.

problems have slowly developed over time', 'As a result of a less severe incident (ie, kneeling, sliding, and/or twisting of the knee or the like)', and 'As a result of a severe incident (ie, during sports, a crash, or a collision or the like)'.

Primary outcome

The primary outcome will be the between-group difference in change in KOOS₄ between the group randomised to meniscal surgery and the group randomised to exercise therapy and patient education from baseline to 12 months follow-up. KOOS₄ is the mean score for the KOOS subscales pain, symptoms, function in sports and recreational activities (Sport/Rec) and quality of life (QOL); the same score was used in a trial comparing surgery to supervised exercise as treatment for ACL tears in patients of similar age as in the present trial.¹⁰ KOOS subscale scores range from 0 (worst) to 100 (best).^{23 24} KOOS is a validated knee-specific questionnaire used to assess patient-reported outcomes in the continuum from knee injury (including meniscal tears) to osteoarthritis and is widely used across the world.²³⁻²⁵

Secondary outcomes

KOOS subscales

To allow for clinical in-depth interpretation, the primary outcome will be complemented by the five individual KOOS subscales (ie, including the fifth subscale—activities of daily living (ADL) subscale).^{23 24}

Western Ontario Meniscal Evaluation Tool (WOMET)

WOMET^{26 27} is a meniscus specific valid, reliable and responsive patient-reported outcome measure that will be used to complement the KOOS score.

Physical performance

Isometric muscle strength will be assessed using the reliable and valid FysioMeter,²⁸ functional performance measured using the maximum number of knee-bends in 30 s, the one-leg hop for distance and the 6 m timed hop

previously applied in trials comparing meniscal surgery to exercise.⁷ The two hop tests will only be assessed at 12 months due to risk of re-injury.

Adverse events

Adverse events (AE) and serious adverse events (SAE) will be recorded at all follow-ups by asking patients about potential AEs using open-probe questioning to ensure that all AEs are recorded. Furthermore, the medical records from the participating hospitals will be checked at the primary endpoint (12 months) for all AEs occurring from inclusion until the 12 months follow-up. An AE is defined as any undesirable experience during follow-up leading to contact with the healthcare system (general practitioner or hospital). If an AE result in hospitalisation, prolonged inpatient hospital care, result in re-surgery, or if an AE is life-threatening, result in death, permanent disability or damage, they will be categorised as SAEs.²⁹ SAE will include cardiovascular or gastrointestinal events, pulmonary embolism, systemic or local infection (or treatment with antibiotics) and deep vein thrombosis, but also other AEs adhering to the definition above will be categorised as an SAE. Crossover to surgery will not be considered as an adverse event as the study is comparing two treatment strategies: early surgery or early exercise and education with the possibility of later surgery. However, crossover to surgery will be registered and reported as it is important when evaluating the clinical applicability of the results. AEs will be categorised into index knee or other sites and will be recorded and assessed for severity by the adjudication committee independent of whether or not there is a causal relationship with study treatments. For all AEs, date of healthcare system contact will be registered. Furthermore, duration of SAEs and potential consequences of SAEs will be assessed.

Other outcomes measures

EQ-5D-5L

General health will be assessed using the reliable and valid EQ-5D-5L questionnaire (5-level version), both the descriptive index and the EQ-VAS.^{30 31} This will also allow for a later cost-effectiveness analysis.

Physical activity and sports

Information on physical activity level³² and participation in sports (Tegner activity scale)³³ will be collected.

Pain location

Patients are asked about pain in other body parts than the knee during the last week with the categories: foot or lower leg, thigh and hip, back, neck or shoulders and arm or hand, all answered by 'yes' or 'no'.

Symptoms of catching and locking

Patients will report the presence and frequency of mechanical knee symptoms (ie, the sensation of catching and locking) based on the question: 'How often have you experienced catching or locking of the knee that is about to undergo treatment?' with five response options ranging from 'never' to 'daily'.

Knee instability

Patients will report the presence and frequency of knee instability based on the question: 'In the last month, have you felt that your knee was unstable or was about to buckle' with six response options ranging from 'never' to 'all the time'. Subsequently, the patients are asked to what extent the knee instability have affected their daily activity level in the last month answered by one of six response options ranging from 'my knee is not unstable or about to buckle' to 'the symptoms keeps me away from all activities of daily living'.

Global perceived effect, patient acceptable symptom state and treatment failure

Global perceived effect (GPE) will be assessed with the question: How are your knee problems now compared with before you entered this study? Answered on a seven-point Likert scale ranging from 'Improved, an important improvement' to 'Worse, an important worsening'. Satisfaction with current knee function (ie, patient acceptable symptom state (PASS)) will be assessed with the question: "When you think of your knee function, will you consider your current condition as satisfying? By *knee function*, you should take into account your activities of daily living, sport and recreational activities, your pain and other symptoms and your quality of life'. Answered by 'yes' or 'no'. This question has previously been used to assess PASS³⁴ in patients with knee injury.³⁵ Participants not satisfied with current knee function (ie, answering 'no' to the PASS question) will be asked to complete a second single-item question, relating to treatment failure (TF) at the 12-month follow-up: 'Would you consider your current state as being so unsatisfactory that you think the treatment has failed?'. Answered by 'yes' or 'no'.³⁵

Pain and function during follow-up

Using SMS, all patients in the RCT will receive a questionnaire each week during the first 3 months and after that each month until the 12 months follow-up with questions from the subscale Sport/Rec from the KOOS^{23 24} and a question regarding pain intensity when ascending/descending stairs and a question regarding pain intensity during sitting/lying on a 11-point Numeric Rating Scale (NRS).³⁶ Patients in the observational cohort will only receive the SMS monthly until the 12 months follow-up. Patients in the group randomised to exercise and education will, in addition, register pain intensity on a 11-point NRS³⁶ before and after each of the supervised exercise sessions.

Treatment-related outcomes

Information on knee pathology and type of surgery

Information about location of tear, type of tear and type of treatment (repair or resection) will be collected using an expanded version of the International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS) classification of meniscal tears questionnaire by the operating surgeon,³⁷ including International Cartilage Repair Society (ICRS) grading of cartilage damage.³⁸ This will be supplemented with data from surgery reports on specific pathological findings and surgical procedures carried out.

Compliance, exercise level/intensity and other treatments received during the study

Compliance with the supervised exercise sessions (ie, number of sessions out of 24 possible sessions) and progression of the exercises will be registered for patients in the group randomised to exercise and education. Poor compliance is defined as participating in less than 18 of the 24 exercise sessions. Any participation in supervised exercise postsurgery will be self-reported using an online questionnaire in the group randomised to surgery. Surgery of the knee during follow-up will be registered through a review of the medical records.

Furthermore, patients will be asked to report other treatments related to the knee that they received during follow-up.

Data management

The data collection and management procedures have been approved by the Danish Data Protection Agency (University of Southern Denmark, 16/45314). Personal information about patients will be kept separate from the main dataset and will not be shared. All personal data will be stored securely in order to protect confidentiality before, during and after the trial. Data entry and coding of the de-identified data will be conducted by trained staff at the University of Southern Denmark.

Data monitoring

The study will not have a formal data monitoring committee as adverse events of treatments are well known due to their wide application in the healthcare sector.

Any unexpected serious adverse events or outcomes will be discussed by the trial management committee (identical to the authors of this protocol). Furthermore, the trial management committee will monitor recruitment, treatment and attrition rates and any concerns related to the study.

Adjudication committee

An adjudication committee, comprising members with prior adjudication experience, will independently adjudicate all adverse events in the RCT as to whether they are serious adverse events or not and categorise them into subcategories. They will each receive the adverse events in raw format after the last patient has undergone the 12 month follow-up. Any disagreements between the adjudication committee members will be resolved by consensus. If consensus cannot be reached, additional information will be requested from the hospitals.

Sample size calculation

The study will be powered to detect a difference in change of 10 points between the surgical and non-surgical group in the primary outcome (KOOS₄) from baseline to 12 months follow-up. A 10-point difference in change between groups in KOOS₄ is considered clinically relevant and a similar cut-off has previously been used in trials comparing surgery for different knee pathologies to non-operative treatment.^{10 14 39} To detect this difference, 59 patients in each of the intervention groups is needed (assuming a common SD of 16.5, power=90%, alpha level=0.05). We plan to recruit a total of 140 patients to account for loss to follow-up (19%). Based on Danish National Patient Registry data from 2013 to 2014, more than a total of 800 primary meniscal procedures are carried out in patients aged 18–40 years at the participating recruitment sites. Patients for the observational cohort will be included consecutively until inclusion in the RCT has been completed or until 1000 patients has been included.

Stopping rule

If the intended sample size is not reached at 30 months after recruitment has started at all participating hospitals, the inclusion of patients will stop at 106 patients, which will ensure a power of 80% anticipating 20% loss to follow-up.

Statistical analysis

Between-group comparisons of change from baseline to 1 year follow-up in the primary and secondary continuous outcomes (ie, KOOS, WOMET, muscle strength, knee-bend test and jump performance) will be analysed using a repeated measures mixed model with patients as random effect, visit (baseline, 3, 6 and 12 months) and treatment arm (meniscal surgery or exercise and education) as fixed effects, and with adjustment for baseline imbalance and randomisation stratification factors, that is, hospital and gender. No imputation will take place. A CI excluding 10 points or more in the KOOS₄ score will be interpreted

as a lack of a clinical meaningful difference. Differences in the trajectories of KOOS₄ scores from baseline to 12 months will be analysed using a random slopes and intercepts model. The occurrence of adverse events will be compared between groups at the 1 year follow-up using a Poisson regression model with a robust error variance.⁴⁰ Categorical secondary outcomes will be analysed using χ^2 test, Fisher's exact test or Mann-Whitney U test as appropriate.

All randomised patients will be included in the intention to treat analysis and in the safety analysis. Per protocol and as-treated analyses will be performed for the primary outcome. Those who crossover to surgery or have poor compliance with the exercise in the exercise and education group and those who do not undergo surgery in the surgery group are excluded from the per protocol analysis, while the as-treated analysis is expected to have three groups, that is, including the group crossing over to surgery in addition to the original two randomisation groups.

A detailed statistical analysis plan will be made publicly available before unblinding the data and any analyses are performed.

ETHICS, DISSEMINATION AND PERSPECTIVES OF THE STUDY

Ethics and auditing

The study is approved by the Regional Committees on Health Research Ethics for Southern Denmark (S-20160151) and will be conducted in agreement with the Helsinki declaration. Informed consent material is available in Danish with the approved protocol. If a patient sustains any trial-related harm they are covered by Danish law. The Regional Committees on Health Research Ethics are annually selecting a number of studies for auditing. The audit process is independent of investigators and sponsors.

Dissemination and protocol amendments

The primary RCT results will be submitted for publication to an international, peer-reviewed journal, regardless of whether the results are positive, negative or inconclusive in relation to the study hypothesis. Authorship eligibility will be based on the recommendations from the International Committee of Medical Journal Editors (ICMJE).

Any important protocol amendments will be reported to the Regional Committees on Health Research Ethics for Southern Denmark, registered at ClinicalTrials.gov and communicated in the primary RCT report.

Perspectives of the study

The results of this RCT will either provide high-quality evidence supporting a practice of early meniscal surgery for young adults aged 40 years or younger with meniscal tears or support a practice of initial supervised exercise therapy and patient education with the option of later surgery if needed in some patients. Either way, the results will provide scientific support for doctors and patients



when discussing the optimal treatment option for the individual patient.

Author affiliations

¹Department of Sports Science and Clinical Biomechanics, Research Unit for Musculoskeletal Function and Physiotherapy, University of Southern Denmark, Odense, Denmark

²Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals, Slagelse, Denmark

³Department of Sports Traumatology, Aarhus University Hospital, Aarhus, Denmark

⁴Department of Orthopaedic Surgery, Sports Orthopedic Research Center—Copenhagen (SORC-C), Copenhagen University Hospital, Copenhagen, Denmark

⁵Department of Orthopaedic Surgery, Aalborg University Hospital, Aalborg, Denmark

⁶Department of Orthopaedic Surgery, Lillebælt Hospital in Kolding, Kolding, Denmark

⁷Department of Regional Health Research, University of Southern Denmark, Odense, Denmark

⁸Department of Orthopaedic Surgery, Næstved Hospital, Næstved, Denmark

⁹Department of Orthopaedics and Traumatology, Odense University Hospital, Odense, Denmark

Twitter Follow Søren T. Skou at @STSSkou and Jonas B. Thorlund at @jthorlund.

Acknowledgements We thank the Orthopaedic surgeons and other healthcare personnel involved in the recruitment, test and treatment of patients at the Department of Orthopaedic Surgery, Copenhagen University Hospital, Amager-Hvidovre; the Department of Orthopaedic Surgery, Lillebælt Hospital in Kolding; the Department of Orthopaedic Surgery, Næstved Hospital; the Department of Orthopaedics and Traumatology, Odense University Hospital; the Department of Orthopaedic Surgery, Aalborg University Hospital and the Department of Sports Traumatology, Aarhus University Hospital and physiotherapists treating patients in the exercise and education group from Arkadens Fysioterapi, Benefit Hobro, Brønshøj Fysioterapi & Træningscenter, Charlottehøj Fysioterapi, FabrikkenSlagelse, Fysikken Ringsted, Fysio Danmark Holbæk, Fysio Danmark Odense, Fysioterapi & Træningsklinik Frederiksberg, Fysioterapi & Motion Hvidovre, Fysiovej, Fysium Næstved, Faaborg Fysioterapi, Guldborgsund Kommune, Kolding Fysioterapi, Middelfart Fysioterapi and Aars Fysioterapi. Statistical consultant for study planning and final data analysis is Professor Jonas Ranstam. Central study coordinator is Anne Marie Rosager. Study advisory board to consult on study planning, results interpretation and other relevant matters: Ewa Roos, University of Southern Denmark; Stefan Lohmander, Lund University; Teppo Järvinen, University of Helsinki; Martin Englund, Lund University; Andrew Carr, University of Oxford.

Contributors STS and JBT conceived the trial and led the development of all procedures including intervention design (exercise intervention and patient education), data management and statistical analyses and drafted the first version of the manuscript. ML, PH, HPJ, CJ, MA and UJ provided feedback on the study, led setup of procedures and data collection at the recruiting hospitals. All authors provided critical intellectual input to the manuscript and read and approved the final version of the manuscript, agreeing to be accountable for all aspects of the work.

Funding The study is funded by the Danish Council for Independent Research (DFF-6110-00045), IMK Almene Fond, The Lundbeck Foundation, the Spar Nord Foundation, the Danish Rheumatism Association, The Association of Danish Physiotherapists Research Fund and The Research council at Næstved-Slagelse-Ringsted Hospitals. The funders have no role in the design of the study and will not have any role in its execution, data management, analysis and interpretation or on the decision to submit results for publication.

Competing interests STS is one of the founders of Good Life with osteoarthritis in Denmark (GLA:D), which is a non-profit initiative hosted at University of Southern Denmark. STS is Associate Editor for Journal of Orthopaedic and Sports Physical Therapy. The authors affirm that they have no other competing interests.

Patient consent Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

Ethics approval The Regional Committees on Health Research Ethics for Southern Denmark.

Provenance and peer review Not commissioned; externally peer reviewed.

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Søren Thorgaard Skou, Martin Lind, Per Hölmich, Hans Peter Jensen, Carsten Jensen, Muhammad Afzal, Uffe Jørgensen and Jonas Bloch Thorlund

BMJ Open 2017 7:
doi: 10.1136/bmjopen-2017-017436

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